REMARKS

The Office Action mailed February 14, 2005, has been carefully reviewed. The amendments made as directed above are in response thereto and further in response to Examiner interview held May 11, 2005, which Applicants gratefully acknowledge.

Claims 24, 26, 28-31, 33-40, 43-45, 47-53 are currently amended; claims 25, 41 and 42, are deleted and claims 56-58, are added.

Claims 24-55 stand rejected under 35 U.S.C § 103 (a) as allegedly obvious over DE 4021082.

Claims 24-55 stand rejected under 35 U.S.C § 103(a) as allegedly obvious over DE 4021082 in combination with EP 0158444 or DE 195 20 659 or Boni (U.S. 5,820, 848)..

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Reexamination, reconsideration, and allowance of the present application are respectfully requested in view of the foregoing amendments and the following additional remarks.

Rejections Under 35 U.S.C. § 103(a)

Claims 24-55 stand rejected under 35 USC 103(a) as being unpatentable over DE 4021082. The Examiner asserts that DE 4021082 discloses skin treatment compositions containing liposomal gels and that the gels contains a phosphotidylcholine (10%), alcohol ().1 – 20%), inositol (0.1-10%) and the rest water.

The Examiner further acknowledges that DE does not teach all of the claimed ranges for the components; does not teach the use of glycerol or ethanol, does not teach the use of buffers, does not teach the mixing of components in an inert gas atmosphere.

As previously explained, the Examiner's characterization of DE 40210982 is in error.

DE 40210982 teaches and claims skin treatment agents containing a bilayer source, salts of organic acids, alcohol, a stabilizer and lipids. The present invention does not teach the use of salts of organic acids, nor of lipids, nor a stabilizer within the asserted meaning of those terms in DE 40210982. In particular, there is no teaching or suggestion, nor is it within the skill of an artisan that withholding salts of organic acids and lipids on the basis of the teachings or suggestions of DE 40210982 would lead to the phospholipid gels of the present invention having its unexpected results.

Morever, DE 40210982 teaches that stabilization of phosphotidylcholine compositions against auto-oxidation is problematic and that while ordinary anti-oxidants such as vitamins C and E may stabilize compositions having 0.1 to 2% by weight of phosphatidylcholine, stability against auto oxidation is difficult to achieve at contents of 2-10 wt % phoshpatidylcholine. (See page 4, paragraph 4). As stabilizers against auto-oxidation, DE 40210982 teaches the use of urea and or monosaccharides such as inositol. (See page 9, paragraph 2). If anything, DE 40210982 teaches away from the use of phospholipids comprising greater than 10 wt % of the formulation because of the danger of auto-oxidation.

There is no teaching or suggestion that on the basis of DE 40210982 , one could raise the phospholipid compositions to amounts well in excess of 10 % up to about 60%, and additionally withhold the use of lipids and salts of organic acids which were taught by DE 40210982 as necessary ingredients, and arrive at the present invention.

Further nowhere was it taught or suggested that the phospholipid formulation having much greater than 10% to about 60% phospholipid can be stabilized against liquefaction by the use of tetrahydric, pentahydric, hexahydric and sugar alcohols.

In particular, known phospholipid gels have the disadvantage that they can liquefy on incorporation of a pharmaceutical, buffer or salt, in particular, if readily soluble substances such as diphenhydramine HCl are incorporated. In these cases, the preparations may flow even under their own weight. Therefore, an object of the instant invention was to provide a phospholipid gel having a high stability on application to the skin and in the presence of an incorporated pharmaceutical, buffer or salt.

Accordingly, Applicants found that this problem can be solved by incorporating into the phospholipid gel a tetra-, penta- or hexahydric alcohol and or sugar, thus stabilizing the gel against liquefaction as demonstrated in examples 3-5 of the instant application.

Despite the deficiencies of DE 40210982 in relation to the present invention, Applicants' claims exclude the components such as organic acids, lipids and stabilizers taught by DE 40210982 using "consisting essentially of" to recite ingredients differing very much in content and concentration from the recitals of DE 40210982. In addition, independent claim 24 has been narrowed by specifically enumerating the class of pharmaceutically active compounds or cosmetically active compounds in a manner that excludes urea, claimed by the Examiner to have possible pharmaceutical action. All other claims depending from or else incorporating all the limitations of claim 24, Applicants assert that the claims of this application are free and clear of DE 40210982 and respectfully ask the Examiner to withdraw this ground for rejection.

Also, claims 24 - 55 stand rejected under 35 U.S.C. § 103(a) as unpatentable over DE 4021082 in view of EP 0158444 or Boni (U.S. 5, 820, 848) or DE 195 20 659. According to the Examiner, what is lacking in the teachings of DE 40210982 is the teaching of higher amounts of phospholipids and the use of buffer and the use of inert atmosphere to prepare phospholipid formulations. Applicants disagree and traverse as follows.

As amended, the deficiencies in DE 40210982 extend not only to the higher concentration of phospholipid, but to the exclusion of DE's organic acids, lipids and stabilizers. Those deficiencies are not cured by the combinations which the Examiner now asserts.

In the first place, DE 40210982 and EP 0158444 are not even properly combinable. Whereas DE 40210982 teaches skin treatment compositions comprising phospholipids stabilized against auto-oxidation, EP 0158444 teaches pro-liposomal formulations comprising phospholipids capable of forming liposomes when **agitated in excess water** and for use as drug carrier. Thus, while DE 40210982 is concerned with cosmetic applications in topical media, EP 015844 is concerned with drug delivery applications in biological fluids. Applicants assert that there would be no motivation or suggestion to apply the use of buffer and inert atmosphere of EP 0158444 in DE 40210982 to attempt to arrive at the instant invention. Moreover, the asserted combination would still not arrive at the present invention.

The Examiner asserted that EP 0 158 441 discloses a composition containing 45% lecithin, 36% ethylene glycol or propylene glycol and 0.9% glucose. The Examiner further asserts that EP 0 158 441 teaches the use of phosphate buffer of pH 7.4, prepared in N_2 atmosphere, and that the drugs [sic] taught are insulin.

EP 0 158 441 teaches a pro-liposomal formulation which spontaneously forms vesicles or liposomes in the presence of **excess water** comprising at least one membrane lipid, at least one water-miscible organic liquid which is a solvent for the lipid, and up to 40% by weight of water. In particular, EP 0 158 441 provides a pro-liposome composition and a method of converting that to an **aqueous liposome dispersion** by addition of aqueous fluid with agitation. (See page 4, lines 11-14). The liposomal dispersion of EP 0 158 441 is stated to be of use as carriers of compounds having biological property. (See page 9, lines 23-25). As pointed out to the

Examiner and as acknowledged by the Examiner, EP 0 158 441 does not teach the use of glucose as a component of the liposomal formulation, instead, glucose was used to model the drug entrapping properties of the liposomal dispersion. Insulin was also mentioned as an example of a biologically active compound capable of being entrapped by the liposomal dispersion of EP 0 158 441. It is therefore more apropos to state that EP 0 158 441 teaches a pro-liposomal composition capable of, and demonstrably entrapping glucose than to assert, with all due respect, that the pro-liposomal composition of EP 0 158 441 contains glucose or insulin, within the meaning of the present invention. The glucose which the Examiner asserts to be taught by EP 0 158 441 is extrinsic, as in not being an integral part of the pro-liposomal composition of EP 0 158 441. In particular, it is useful to think in terms of how much glucose is trapped within the liposomal vesicles and how much glucose exist in the extra-liposomal space.

In contrast, the present invention discloses a phospholipid gel, which is stabilized against liquefaction by adding a tetrahydric, pentahydric or hexahydric alcohol or sugar. In that sense, the tetrahydric, pentahydric or hexahydric alcohol or sugar alcohol is an integral component of the phospholipid gel of the present invention used to stabilize the phospholipid gel of the present invention against liquefaction. In contrast, the pro-liposomal composition of EP 0 158 441 is designed to be used in a liquefied media.

Moreover, EP 0 158 441 teaches the use of "water miscible liquid which is a solvent for its membrane lipid," preferably an aliphatic alcohol such as glycerol, propylene glycol, ethanol, isopropyl alcohol, methanol, butanol, ethylene glycol. (See page 6, lines 10 – 15). There is no teaching or suggestion anywhere in EP 0 158 441 that the "water miscible liquid which is a solvent for its membrane lipid" must contain at least one dihydric or trihydric C_2- C_4 alcohol and at least one polyhydric alcohol. Applicants fail to find support for the Examiner's assertion that

the glucose allegedly "contained" in EP 0 158 441 should be construed other than liposome-entrapped glucose as taught by EP 0 158 441.

In any case, since claims 24 – 55 are now free and clear of DE 4021082, the asserted combination fails and there is no basis for maintaining this ground for rejection. As for Boni (5,820, 848) and DE 195 20 659, cited by the Examiner as teaching high levels of phospholipids contents and alcohol, their combination with DE 4021082 fails because the asserted combination must necessarily contain the organic acids, lipids and stabilizers of DE 4021082 which are excluded by the claims of the present invention. Again, this ground for rejection is now moot in view of the amendments now made and its withdrawal is respectfully requested.

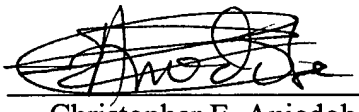
CONCLUSION

In view of the foregoing, Applicants submit that there is no basis for applying the previous rejections to the pending claims and withdrawal of the rejections is respectfully requested. The claims are believed to be in condition for allowance, and Applicants earnestly solicit from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, he is invited to contact the undersigned at his earliest convenience.

Respectfully submitted,

REED SMITH LLP

By: 

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